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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/770,712	02/03/2004	Aristo Vojdani	IMSCI2.008A	2285

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EXAMINER	
CHEU, CHANGHWA J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/770,712	VOJDANI, ARISTO	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/7/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

Etiology

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 1-30 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The instant invention directs to a method for determining etiology of an autistic spectrum disorder in a patient, comprising the steps of:

a) determining a level of at least one infectious agent derived antigen or antibody against an infectious agent derived antigen, at least one toxic chemical derived antigen or an antibody against a toxic chemical, and at least one dietary protein derived antigen or antibody against a dietary protein, in one or more samples from the patient;

b) comparing the level of antigens and/or antibodies determined in step. a) with a normal level of the antigens and/or antibodies from control subjects, wherein the increase level of said antibodies or antigens indicates a likelihood of the autistic spectrum disorder based on the presence of the antigens.

The state of art involves immunoassay for the detection of the related antigens/or antibodies from autistic patients compared with the healthy ones.

In light of the clinical data in the specification, nevertheless there is insufficient data to enable one ordinary skill in the art to use the claimed invention to decipher the real mechanism(s) causing the autistic disease.

Etiology is medically defined "the cause of the disease" (See New Riverside University Dictionary (1994)- note applicant does not define such term in the specification).

The overall clinical data reported by applicant mainly indicate there is a correlation of certain elevated levels of antibodies (or antigen) in the autistic patients compared to the normal control group (See Example 1 to Example 3). Examiner acknowledges these data somehow indicating a correlating relationship between the existing patients, namely autistic syndrome, and the increase level of certain autoantibodies, i.e. IgA, IgG and IgM. However, correlation per se cannot be equated to etiologically causal factor. Nexus is not necessarily true for causation. At best, the current data may be in support of diagnosing autistic patients, but not determining etiology.

Examiner would like to draw applicant's attention in the following excerpts from the specification.

(Section 0230)

*It is **likely** that environmental factors including infection-induced injury causes release of neuronal antigens, which through activation of inflammatory cells, could lead to autoimmune reactions in genetically susceptible individuals. **However, only long-term studies can prove** the protective versus pathogenic role of these antibodies in children with autism.*

(Section 0256)

*To our knowledge, our analyses are the first to clearly demonstrate that dietary peptides, bacterial toxins and xenobiotics bind to lymphocyte receptors and/or tissue enzymes. This results in autoimmune reactions in children with autism. We **suggest** that these findings* provide a **mechanism** *by which environmental factors modulate the immune system and should help us develop preventive and therapeutic methods to reduce dietary peptides, bacterial toxins and toxic chemical-induced autoimmune reaction in autism.*

At most, in light of the data and explanation, it would be reasonable to conclude that the instant claimed invention is at preliminary stage endeavoring to determine the true cause or true etiological causation of the autistic disease.

Furthermore, claim 1 recites determining a combination of at least 3 categories of antigen/antibodies, namely infectious agents, toxic chemicals, and dietary proteins, **simultaneously** (emphasis added)(note, the language is **not** a Markush selection). From practical experimental point of view, this methodology would cause confusion and may obfuscating the purpose. Usually one ordinary artisan in the field would determine **one** target factor (or variable**) at one time** to ensure the reliability and reproducibility of the overall experimental design (emphasis added). Concomitant determining two other variables may result in misleading the results because one may encounter dilemma to decide which one is the real causation factor.

In view of the aforementioned lack of predictability in the art, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success,

absent a specific and detailed description in the applicant's specification of how to effectively practice the recited method and absent working examples.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claim 20-21, 24-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Vojdani et al. (J Neuroimmunology 2002 Vol. 129, page 168, applicant submitted IDS on 5/7/2004).

Vojdani et al. teach a method of determining possible causes for autistic disease in children. Vojdani et al. teach determining levels of antibodies derived from infectious agents, Chlamydia pneumoniae or streptococcal M protein, or dietary peptide milk butyrophilin in patients, and the elevated levels of the said antibodies maybe the cause of the autistic disease (See page Abstract).

With respect to claim 24-25, the results are reflected to the autistic spectrum disorder. Supra.

With respect to claim 26-27, the data show the levels of antibodies in autistic patients are higher than the normal population for at least two standard deviation (See Figure 6).

With respect to claim 28-29, Vojdani et al. teach using immunoassay ELISA for the detection of the antibodies (See Materials and Methods).

With respect to claim 30, Vojdani et al. teach detection of IgG, IgA and IgM (See Table 1).

5. Claim 1-9, 11-15, 17-22, 24-26, 28-30 are rejected under 35 U.S.C. 102(a) as being anticipated by Cooper et al. (Internatl J Immunopathology and Pharmacology 2003 Vol. 16, page 289- applicant submitted IDS on 5/7/2004).

Cooper et al. teach a method of determining possible causes for autistic disease in children. Cooper et al. teach determining levels of antibodies derived from infectious agents, or toxic chemicals or dietary proteins in patients, and the elevated levels of the said antibodies maybe the cause of the autistic disease (See page 290-291).

With respect to claim 2-3, the infectious agents are streptococcus or viral agents or Chlamydia pneumoniae (See page 290, right column, first paragraph).

With respect to claim 4 and 12, the chemical toxic agent also includes lead or mercury (See page 290, right column, third paragraph).

With respect to claim 5 and 11, the dietary peptide includes milk butyrophilin (See page 290, right column, first paragraph).

With respect to claim 6, 8 and 22, the self-tissue antigen includes CD13 antigen involving specifically binding on lymphocytes. Surpa.

With respect to claim 7 and 21, the peptide is selected from cell antigen or receptor. Surpa.

With respect to claim 9, the peptide also is a neurotransmitter, such as opioid peptides (See page 291, left column, first paragraph).

With respect to claim 13-14, 24-25, the detection of the specific antibodies are linked to the occurrence of autistic disease. Supra.

With respect to claim 17-19 and 29-30, Cooper et al. teach using immunoassay ELISA to detect IgA, IgM and IgG in comparison of both autistic patients and normal ones. Surpa.

6. Claim 1-8, 10-30 are rejected under 35 U.S.C. 102(a) as being anticipated by Vojdani et al. (Internatl J Immunopathology and Pharmacology 2003 Vol. 16, page 189- applicant submitted IDS on 5/7/2004).

Vojdani et al. teach a method of determining possible causes for autistic disease in children. Vojdani et al. teach determining levels of antibodies derived from infectious agents, or toxic chemicals or dietary proteins in patients, and the elevated levels of the said antibodies maybe the cause of the autistic disease (See page Abstract).

With respect to claim 2-3, the infectious agents are streptococcus streptokinase. Surpa.

With respect to claim 4 and 12, the chemical toxic agent also includes ethyl mercury. Surpa.

With respect to claim 5, the dietary peptide includes gliadin and casein. Surpa.

With respect to claim 6, 8 and 22, the self-tissue antigen includes CD26 and CD69 antigen involving specifically binding on lymphocytes. Surpa.

With respect to claim 7 and 21, the peptide is selected from cell antigen or receptor. Surpa.

With respect to claim 10, the peptide is selected from dipeptidylpeptidase IV (See Method and Materials).

With respect to claim 11, the infectious agent is selected from streptokinase (See Abstract).

With respect to claim 13-14, 24-25, the detection of the specific antibodies are linked to the occurrence of autistic disease (See Table I-II and Figure 1-2).

With respect to claim 17-19 and 29-30, Vojdani et al. teach using immunoassay, e.g. ELISA, to detect IgA, IgM and IgG in comparison of both autistic patients and normal ones (See Materials and Methods).

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

May 18, 2006

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